REMARKS

As noted above, the present amendments to the claims are based on a telephonic discussion with Supervisory Primary Examiner James Housel. Examiner Housel indicated to the undersigned that the Office would, in view of a discussion of *In re Johnson and Farnham*, 194 USPQ 187 (CCPA 1977) (hereinafter, "*Johnson*") consider amendments throughout the claim set that recite that heterologous sequences were "non-coxsackievirus" (corresponding to currently rejected claims 73-78 and claims cancelled earlier during prosecution). Applicants thank Mr. Housel for this consideration and information.

The following claims are currently being amended or cancelled:

(A) Pending claims 1, 17[2], 18 and 73 are amended.

(B) Withdrawn claim 72 is also amended to bring it into correspondence with amended claim 1.

(C) Claims 74 -78 are hereby cancelled without prejudice or disclaimer (as their language is now identical with that of claims 1, 18, 3, 7[3] and 13, respectively, in view of the amendments noted in (A) above) and discussed below.

All the amendments are supported by the original claims and the specification throughout. No new matter is added by these amendments. Entry and allowance of the amended claims is respectfully requested.

I. Withdrawal of Earlier Rejections

Applicants acknowledge and thank the Examiner for withdrawing certain of the prior rejections. Specifically, a rejection of Claims 1, 3, 18 and 20-22 under 35 U.S.C. 112, first paragraph, was withdrawn in view of Applicant's amendment to the claims specifying the region in which the heterologous nucleic acid is inserted. Rejection of claims 13-15 and 28 under 35 U.S.C. 112, second paragraph, was withdrawn in view of Applicant's persuasive remarks further clarifying the claim language.

---

[2] The amendment of claim 17 is for clarity of language, and not of the nature of the other amendments being made here. Specifically, "insert" is being replaced with "inserted heterologous nucleic acid".

[3] The actual language of Claims 3 and 7 is not being changed; rather, they depend from claims being amended herein.

II. Discussion of Pending Rejections under 35 USC §112, First Paragraph and §102(b)

A. Rejection Under 35 U.S.C. 102(b) Over Caggana

Claims 1, 3, 6-12, 18, 20-22, 24-27, 30-33 and 73 were rejected under 35 U.S.C. 102(b) as anticipated by Caggana *et al.* (J. Virol., 1993, 67:4797-4803, herein, "Caggana").

The claims are drawn to various recombinant attenuated coxsackievirus B4 virions containing heterologous inserts, nucleic acids encoding the recombinant attenuated coxsackievirus B4 virions with the inserts. The heterologous inserted nucleic acids encode T cell and/or B cell epitopes, *etc.* The claim language was said to be encompassed by an embodiment disclosed in Caggana, which has been discussed at length in the preceding Actions and Responses and will not be reiterated here, because of the nature of the present amendments.

Applicants and the Office remained at loggerheads over the issue of what is the proper interpretation of the term "heterologous" in view of the specification and four expert Rule 132 Declarations that tried to explain the differences between the Office's interpretation of the definition in the specification and the real meaning of this term, interpreted differently, in the world of science and research. The Office maintained its position that the there is no room to interpret the term given the way it was defined in the specification. While Applicants do not accept this position, in view of the approach suggested by Mr. Housel, being followed here, it appears that there is a way out of that conundrum, that would render this prior art rejection moot. This is discussed below.

B. Rejection of "New Claims" 74-78 for Inadequate Written Description (New Matter)

1. The Rejection

These claims were rejected USC §112, first paragraph due to an alleged lack of adequate written description and introduction of new matter based on the use of the language "non-coxsackievirus". Applicants had added a short subset of new claims which re-introduced the previously cancelled language that recites "non-coxsackievirus" when defining the "heterologous" nucleic acids, inserts, polypeptides, *etc.* . claims. The Office Action indicated that these claims lacked adequate written description and introduced new matter.

"Non-coxsackievirus" was said to be a new limitation that is not supported by the specification. The Office recognizes that specification gives examples of epitopes of interest that are not coxsackievirus (*e.g.*, page 19), the Action maintains that the specification does not exclude

coxsackievirus chimerics. Indeed, while there is no explicit exclusion of such a creature, Applicants emphasize the very large number of explicitly disclosed embodiments (some exemplified, some not) of **non**-coxsackievirus chimerics vs the one non-excluded embodiment on which the Office has focused. The specification's definition of "heterologous" is said to clearly encompass nucleic acid that is from another virus that is not the "exact same virus." Applicants find that "exact same virus" is a rather ambiguous term not particularly helpful in addressing the issues around which the present rejections and amendments are centered. Based on various other statements by the Office in the prosecution history, Applicants take this expression to mean any coxsackievirus of the CB4 serotype that differs from the vector virion by a single nucleotide. (That is primarily dealt with in a different context discussed in the Ramsingh-4 Declaration attached hereto and in Section D. below.)

The pending Action notes that in an earlier Office Action, claims 1, 3, 4, 6-15, 17-18, 20-28 and 30-36 had been rejected for reciting this same term for the same reasons. In response to that rejection, Applicants filed arguments (12/3/04) to rebut the rejection, yet also amended the claims to remove the term, "non-coxsackievirus". Since the term has been reintroduced into the claimed invention in new claims 74-78), the arguments Applicants filed in their paper of 12/3/04 were now addressed by the Office.

Applicants had argued that the Office did not cite any precedent supporting its position. Applicant made an assumption (right or wrong) that the Office was or would rely on the Board's opinion in *Ex parte Grasselli,* 231 USPQ 393 (Pat. Bd. App. & Inf. 1983) for its position on negative limitations. Applicants asserted that the facts, issues and reasoning in *Grasselli* do not apply to the present claims. The Office noted that Applicants asserted that this rejection was a classic elevation of "form over substance".

The Office's response in the present Action stated is described in the second paragraph under Sec. B, above. There is no clear statement as to what specific authority the Office relies upon in this rejection, *e.g.*, *Grasselli*, which was the "classic" case used by the Office in the past for making such rejection of claims with negative limitations (or undisclosed subgenuses).

Applicants had earlier taken the position (and do so now) that examples of non-coxsackievirus chimerics in the specification, such as ovalbumin peptides and HIV peptides but also a much larger array of disclosed viruses, other pathogenic microorganisms, parasites, *etc.*, from which heterologous epitopes could be derived, are adequate to support claims directed to CB-4 vectors with inserted *non-coxsackievirus* heterologous DNA.

> An epitope of interest can be an antigen of a pathogen or toxin, or a portion of an antigen of a pathogen of toxin, or prepared from an antigen of a pathogen or toxin, or from another antigen or toxin which elicits a response with respect to the pathogen, or from another antigen or toxin which elicits a response with respect to the pathogen, such as, for instance: a Morbillivirus antigen (e.g., a canine distemper virus or measles or rinderpest antigen such as HA or F; a rabies glycoprotein, such as rabies glycoprotein G; an avian influenza antigen, such as turkey influenza HA, Chicken/Pennsylvania/1/83 influenza antigen such as a nucleoprotein (NP); a bovine leukemia virus antigen, such as gp51,30 envelope; a Newcastle Disease Virus (NDV) antigen, such as HN or F; a feline leukemia virus antigen (FeLV), such as FeLV envelope protein; RAV-I env; matrix and/or preplomer of infectious bronchitis virus; a Herpesvirus glycoprotein, such as a glycoprotein from feline herpesvirus, equine herpesvirus, bovine herpesvirus, pseudorabies virus, canine herpesvirus, HSV, Marek's Disease Virus, or cytomegalovirus; a flavivirus antigen, such as a Japanese encephalitis virus (JEV) antigen, a Yellow Fever antigen, or a Dengue virus antigen; a malaria (Plasmodium) antigen, an immunodeficiency virus antigen, such as a feline immunodeficiency virus (FIV) antigen or a simian immunodeficiency virus (SIV) antigen or a human immunodeficiency virus antigen (HIV); a parvovirus antigen, such as canine parvovirus; an equine influenza antigen; an poxvirus antigen, such as an ectromelia antigen, a canarypox virus antigen or a fowlpoxvirus antigen; or an infectious bursal disease virus antigen, such as VP2, VP3, VP4; a Hepatitis virus antigen, such as HBsAg; a Hantaan virus antigen; a *C. tetani* antigen; a mumps antigen; a pneumococcal antigen, such as PspA; a Borrelia antigen, such as OspA, OspB, OspC of Borrelia associated with Lyme disease such as *Borrelia burgdorferi*, *Borrelia afzelli* and *Borrelia garinii*; or a chicken pox (varicella zoster) antigen).

Specification at pages 19-20

The Office asserted that only claims to CB4 viral vectors of exemplified ovalbumin peptides and HIV peptides would be supported. Without wishing to expand the discussion of this particular issue here, the law of written description does not limit applicants to claims having the scope of exemplified embodiments. (See, for example, a case as recent as Falkner v. Inglis 79USPQ2d 1001-1009 (Fed. Cir. , 26 May 2006, and cases cited therein such as *LizardTech, Inc. v. Earth Resource Mapping, PTY, Inc.* 424 F.3d 1336, 1345 (Fed. Cir. 2005), *Union Oil Co. v. Atl. Richfield Co.*, 208 F.3d 989, 997 (Fed. Cir. 2000); *In re GPAC Inc.*, 57 F.3d 1573, 1579 (Fed. Cir. 1995). Moreover, actual reduction to practice is not required for written description. *See Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 926 (Fed. Cir. 2004) ("We of course do not mean to suggest that the written description requirement can be satisfied only by providing a description of an actual reduction to practice. Constructive reduction to practice is an established method of disclosure..."). The Office's attempt to limit the number of different "non-coxsackievirus" heterologous peptides encoded by the presently claimed CB4 vectors to those exemplified (OVA, HIV) does not comply with the well-established law on this point.

The key issue addressed below is the Office's position that Applicant may not "claim around" the embodiment of coxsackievirus-coxsackievirus chimerics (as represented by the cited Caggana reference) by introducing the limitation of "non-coxsackievirus." However, it is clear that following the telephonic discussions with SPE Housel noted above, and presumably after some internal discussions in the Examining Group, the Office is prepared to consider and allow claims that include this language based on the precedent of *Johnson, supra.*

The pending prior art rejection under §102(b) over Caggana *et al. (Section A, above)*, was directed to claims 1, 3, 6-12, 18, 20-22, 24-27, 30-33 and 73. It should be obvious that the new amended language, which is introduced here into claims 1, 18, 72 (withdrawn) and 73 (and of course into their dependent claims, if any) would distinguish sharply from Caggana and render all the claims free of any cited prior art.

2. **Applicants' Response: Patentability of Claims with Negative Limitations**

Again, the Office Action never made clear whether it relied on specific case law in the present rejection of claims 74-78 for lack of written description/new matter. The law and rules for evaluating negative limitations are described in part in MPEP 2173.05(i); that which is particularly relevant to the present case is discussed briefly below (omitting discussion of §112, second paragraph, issues, which Applicants do not believe are applicable here.

> Any negative limitation or exclusionary proviso must have basis in the original disclosure. If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims. See *In re Johnson*, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977) ("[the] specification, having described the whole, necessarily described the part remaining."). See also *Ex parte Grasselli*, 231 USPQ 393 (Bd. App. 1983), *aff'd mem.*, 738 F.2d 453 (Fed. Cir. 1984). The mere absence of a positive recitation is not basis for an exclusion.

Although a claim containing a negative limitation which lacks basis in the original disclosure fails to comply with the written description requirement, a lack of *literal* basis in the specification for a negative limitation may not be sufficient to establish a *prima facie* case for lack of descriptive support. *Ex parte Parks*, 30 USPQ2d 1234, 1236 (Bd. Pat. App. & Inter. 1993).

As a primary matter, Applicants believe that the Office has not set forth a sufficient *prima facie* case of inadequate written description under § 112. The burden of showing that a claimed invention is not described in the specification rests on the PTO in the first instance, and it is up to the PTO to give reasons why a description not *in ipsis verbis* is insufficient. *In re Wertheim*, 191

U.S.P.Q. 90, 98 (CCPA 1976) ("Lack of literal support...is not enough...to support a rejection under §112.").

In *Ex Parte Parks, supra* the Board described the legal standard and PTO burden for rejecting a claim due to lack of adequate descriptive support:

> **...it is incumbent upon the examiner to establish that the originally-filed disclosure would not have reasonably conveyed to one having ordinary skill in the art that an appellant had possession of the now claimed subject matter.** *Wang Laboratories, Inc. v. Toshiba Corp.*, 993 F.2d 858, 26 U.S.P.Q.2d 1767 (Fed. Cir. 1993). Adequate description under the first paragraph of 35 U.S.C. 112 **does not require literal support for the claimed invention.** In *re Herschler,* 591 F.2d 693, 200 U.S.P.Q. [*5] 711 (CCPA 1979); *In re Edwards,* 568 F.2d 1349, 196 U.S.P.Q. 465 (CCPA 1978); *In re Wertheim,* 541 F.2d 257, 191 U.S.P.Q. 90 (CCPA 1976).

(emphasis added).

In making the present rejection, Applicants believe that the Office has not met its burden in showing how the application does not reasonably convey to a person skilled in the relevant field that, at the time the application was filed, the inventor(s) "*had possession*" of the claimed invention (recombinant attenuated coxsackievirus B4 virion engineered to contain a heterologous non-coxsackievirus nucleic acid inserted ...). Rather, the Office Action only stated the fact that "Non-coxsackievirus" was a "new limitation" not adequately described in the specification and that only two narrow sets of *non-coxsackie* heterologous sequences/peptides (from OVA and HIV viral peptides, that were actually exemplified) could be considered as supported. In other words, Applicants understand the Office to be saying that there are not enough *non-coxsackievirus* embodiments described in the specification to support such a "genus" or subgenus of heterologous sequences. Applicants believe that since the Office has failed to carry its burden as set forth in *Parks,* it should withdraw this ground for rejection.

However, even if, *arguendo*, the Office had made out a sufficient *prima facie* case, Applicants believe that the weight of precedent comes down in their favor in rebutting such a rejection. The *Grasselli* Board took the position that the negative limitations recited in the claims (...catalyst in the **absence of** sulfur and halogen... said catalyst being **free of** uranium and the combination of vanadium and phosphorus), because they did not appear in the specification as filed, introduced new **concepts**, thereby violating the written description requirement of 35 U.S.C. § 112 first paragraph (*Grasselli* at 394). The Board added that:

> the express exclusion of certain elements implies the permissible inclusion of all other elements not so expressly excluded. This clearly illustrates that such negative limitations do, in fact, introduce new concepts.

In the present application, the exclusion of one embodiment (where the *heterologous* sequence comes from a distinct coxsackievirus) does not "introduce new concepts" (see more below). The present case does not involve claim "elements" of the sort found in Grasselli's claim 1, but rather species. If one substitutes "species" for "elements" in the foregoing quote, then amended claim 1 of this case would imply inclusion of all other nucleic acid "species" meeting the limitations set forth in the claim, *i.e.* a *non-coxsackievirus* nucleic acid inserted within the P1 region of the open reading frame of a recombinant attenuated coxsackievirus B4 virion genome which inserted nucleic acid encodes a heterologous (*non-coxsackievirus* polypeptide) which is fused to a capsid protein of the virion. (A similar analysis would apply to the embodiment of claim 13.)

In other words, express exclusion of certain "elements" [here, species – specifically a nucleic acid from a different coxsackievirus] may indeed imply the permissible inclusion of all other elements [species] not expressly excluded - - namely, other heterologous nucleic acid sequences. However, in contradistinction to the Board's commentary in *Grasselli*, what new **concepts** could the exclusion of a nucleic acid sequence of a distinct coxsackievirus in amended claim 1 possibly introduce? In fact, excluding a nucleic acid sequence of a (arguably distinct) coxsackievirus to avoid a prior art reference does not "introduce new concepts." Rather, it underscore the fit of the present facts to the CCPA decision in *In re Johnson*, 194 U.S.P.Q. 187, (1977).[4]

In the *Johnson* case, the CCPA reversed a decision of PTO Board of Appeals affirming the rejection under 35 §§ USC 102 or 103 (the rejection also raising a written description issue under 35 U.S.C. § 112) of various claims. This was a "benefit " case under 35 U.S.C. § 120 in which appellants sought the benefit of an earlier application to antedate a single prior art reference. The inquiry of the *Johnson* court was "whether, after exclusion from the original claims of two species specifically disclosed in the 1963 application, the 1963 disclosure satisfied §112, first paragraph, for the 'limited genus'[20] now claimed." Footnote 20 is noteworthy in that the court adopted the appellant's term "limited genus" over the Board's chosen label of "artificial subgenus."[5] The CCPA noted that "[w]hatever the label, the issue is the same."

---

[4] Applicants believe that any additional statements by the Board in responding to the Request for Reconsideration (*Ex parte Grasselli, et al.*, 231 U.S.P.Q. 395) are not applicable to the present claims, nor is the Board's discussion of various arguments that the *Grasselli* appellants did make or "could have made."

[5] which seems to carry a pejorative tone

In reversing the Board's finding that "no antecedent basis exists in the parent case" for the "limited genus" in claim 1, the court found "more than ample basis for claims of such scope." The court emphasized that (in the early disclosure being relied upon) the appellants had (a) given a number of choices for "E precursor compound," (b) identified a broad class of suitable choices for the "E' precursor compound," and (c) provided a large number of examples that detailed fifteen species of polyarylene polyethers. "Two of the many choices for E and E' precursor compounds are deleted from the protection sought, because appellant is *claiming less* than the full scope of his disclosure." (*Johnson* at 195, emphasis in the original). Citing its earlier decision in *In re Wertheim*, 191 USPQ 90, the court noted that:

> Inventions are constantly made which turn out not to be patentable, and applicants frequently discover during the course of prosecution that only a part of what they invented and originally claimed is patentable. [9] It is for the inventor to decide what *bounds* of protection he will seek. *In re Saunders*, 58 CCPA 1316, 1327, 444 F.2d 599, 607, 170 U.S.P.Q. 213, 220 (1971). To deny appellants the benefit ... would, as this court said in Saunders:
>
> > let form triumph over substance, substantially eliminating the right of an applicant to retreat to an otherwise patentable species merely because he erroneously thought he was first with the genus when he filed.

Johnson at 195, 196

Applicants believe that the foregoing aptly describes the present situation, where the inventors are deciding what bounds of protection they seek after their having "discover[ed] during the course of prosecution that only a part of what they invented and originally claimed is patentable" (according to the Office's current position, not the Applicants'.[6]

In distinguishing the cases relied upon by the Board,[7] the *Johnson* court stated that "...appellants' grandparent application contains a broad and complete generic disclosure, coupled with extensive examples fully supportive of the limited genus now claimed...," noting further that *Welstead* could have been just as easily cited by the Board in support of a contrary decision in view of what the CCPA implied (in *Welstead*) concerning the possibility that "descriptions of species amounting in the aggregate to the same thing may satisfy the description requirements of 35 USC § 112, first paragraph."

---

[6] a position with which Applicants noted above they take issue, but accept in the context of the present amendments to move this case forward to allowance.

[7] Most prominently, *In re Welstead*, 59 CCPA 1105, 463 F.2d 1110, 174 U.S.P.Q. 449 (1972).

In distinguishing *In re Smith*, 59 CCPA 1025, 173 U.S.P.Q. 679 (1972), the *Johnson* court pointed out that the applicant in *Smith* sought to rely on his prior application for a **broadened** generic claim[8] where there was no disclosure of either the range itself or of a sufficient number of species to establish entitlement to the claimed range. In contrast to this, the appellants in *Johnson* were narrowing their claims, and the full scope of the newly claimed limited genus was supported, both generically and specifically.

The instant application also represents a narrowing of an amply described genus (the Office having objected to the excision of a single "embodiment"), and the full scope of the newly claimed "limited genus" is supported, both generically and specifically. The present case therefore falls reasonably within the fact pattern of *Johnson.*

The *Johnson* court's conclusions and holding regarding the legitimacy of removing ("excising") species by proviso is summarized by following statements.

> The notion that one who fully discloses, and teaches those skilled in the art how to make and use, a genus and numerous species therewithin, has somehow failed to disclose, and teach those skilled in the art how to make and use, *that genus minus two of those species*, and has thus failed to satisfy the requirements of §112, first paragraph, appears to result from a hypertechnical application of legalistic prose relating to that provision of the statute. All that happened here is that appellants narrowed their claims to avoid having them read on a lost interference count."

Johnson, at 196 (emphasis added).

Indeed, all that happened in the present case is that Applicants narrowed their claims to avoid having them read on a single prior art disclosure (Caggana) of a short nucleic acid sequence being replaced between two CB4 variant viruses of the same strain. This is analogous to avoiding the lost interference count in *Johnson.*

The *Johnson* court went on to conclude that:

> Here, as we hold on the facts of this case, the "written description" in the 1963 specification supported the claims in the absence of the limitation, and ***that specification, having described the whole, necessarily described the part remaining.*** The facts of the prosecution are properly presented and relied on, under these circumstances, to indicate that ***appellants are merely excising the invention*** **of another,** ***to which they are not entitled, and are not creating an "artificial subgenus" or claiming "new matter."***

Johnson, at 196 (emphasis added).

[8] Replacing the limitation "at least 12 carbon atoms with a new limitation of "8 to 36 carbon atoms"

In the present case, Applicants are "merely excising" a "species" or "embodiment" to which (according to the Office) they are not entitled, and are **not** creating an "artificial subgenus" or claiming new matter.

To summarize, Applicants' believe that the Office has not met its legal burden in making out *prima facie* case under § 112, first paragraph, that the specification lacks adequate written description of the subject matter of the amended claims when "heterologous" is limited to "non-coxsackievirus" species. Moreover, even with a sufficient *prima facie* case, the foregoing remarks support Applicants contention that the Office's position is legally incorrect under *Johnson* and that the claims comply completely with the written description requirement of §112, first paragraph. Applicants therefore request respectfully that this rejection be withdrawn.

C. "Second" Rejection for Lack of Adequate Written Description

Claims 3, 6-15, 17, 20-22, 24-28, 30-36 and 76-78 (namely, all claims that read on the CB4-P virus) were rejected as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Office continues to assert that CB4-P is required to practice the claimed invention as a "necessary limitation for the success of the invention as stated in the claims." As indicated in the Action, as a "required element" it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. An alternate way to satisfy this requirement if the "required element" is not so obtainable or available is by a deposit of coxsackievirus CB4-P under 37 CFR § 1.802 in a recognized deposit facility.

The Office asserted that one cannot practice the claimed invention without the "specifically named" CB4-P coxsackievirus "strain." The specification is said to "provide a method for obtaining a virus that is ***like CB4-P***", the Office asserts that "the specification does not provide a repeatable method for obtaining the CB4-P without some kind of "access" to the CB4-P. The Office believes that this virus is not "readily available" material and notes that deposit of CB4-P would satisfy the enablement requirements because the strain would be readily available to the public to practice the claimed invention. The Action notes that the identifying information set forth in 37 CFR 1.809(d) regarding the deposit should be added to the specification.

Applicants' Response

The Ramsingh-4 Declaration is offered to rebut this ground for rejection. Applicants will not reiterate all the points here that appear in the Declaration. For the sake of brevity, Applicants wish to emphasize that the Office's analysis of this issue has a number of flaws that appear to derive from an inadequately clear understanding of the underlying virology and genetics of these viruses. Perhaps Applicants and Declarants have not done an adequate job of explaining these matters in previous communications. The Ramsingh-4 Declaration makes clear that the CB4-P virus is not some kind of unique entity as the Office seems to believe, and that it is readily available through various avenues. Importantly, the virus can be "created" *de novo* by a synthetic approach that relies upon conventional methods. A person of skill in the art will therefore have access to, and be fully enabled to practice the claims if he/she starts with the virus available from the ATCC (termed JVB but the same as CB4-P), or obtained from another source, or created from a synthetic nucleotide sequence using conventional methods. That virus can be manipulated as described in the application (and summarized as well in the Ramsingh-4 Declaration) to practice the claimed invention without the need to resort to any inventive effort.

Applicants also respectfully remind the Examiner that the Tracy Declaration submitted earlier had a section (#9) devoted to this same issue. Applicants believe that this statement from one of the foremost experts in the coxsackievirus field was not given adequate consideration by the Office, possibly due an inadequate to appreciation of the viral biology and genetics of CB4 and other coxsackieviruses.

Tracy stated that

> Viruses that are genetically *equivalent* to CB4-P can be manipulated genetically per the application to allow insertions of heterologous nucleic acids in defined spots as described ... or inserted in-frame and directly upstream of VP4 coding sequences... I know of no reason why one could not use, therefore, any strain of CB4 (or any of the 6 CB serotypes), to produce the chimerae described by the Applicants. There is no reason that a skilled person would be limited in his/her ability to practice this invention using CB4-P or any other CB4 virus. Any genetic variant of the JVB strain of the CB4 serotype can be used in the very same way. JVB is publicly available from the ATCC. Thus, the skilled person would not have to resort to any other deposits of CB4-P virus to practice this invention fully. Moreover, there is nothing special about the serotype B4 versus the other five CB serotypes. Once a person skilled in the field has been apprised of the present invention and read the application, that person will be able to practice it as written in the claims. Indeed, what works in CB4-P to create a virus expressing a heterologous polypeptide that can act a as an immunogen would also work in CB4-JVB or CB4-V (notwithstanding other considerations like virulence). Indeed, what works in CB4-P would also work in any strain of virus of the other coxsackievirus B serotypes.

Applicants request that the Office reconsider these statements along with the Ramsingh-4 Declaration and consider the fundamental biology and genetics of these viruses that have been pointed out. In view of these documents and upon a suitable scientific "review" of coxsackievirus biology, it would be proper to withdraw this ground for rejection and the requirement for a patent deposit of a virus of the CB4-P (JVB) strain.

III. Personal Statement to Examiner Chen

The undersigned wishes to state for the record that he is unaware of what behavior on his part caused the Examiner to be personally insulted. There is no question that the undersigned has attempted to zealously represent his clients in this prosecution, which has been very complex, drawn out and costly (including turnover of examiners, etc.). There is also no question that the Applicant has been frustrated with the course of this examination process. Neither the Applicants nor the undersigned sought to avoid being blunt in pointing out what they considered to be errors, omissions misunderstandings, etc., on the part of the Office. Notwithstanding the foregoing, as a matter of principle and personal style, the undersigned believes that he comports himself in a professional, even an excessively friendly, manner in his personal interactions with patent examiners and other PTO personnel, and is unaware how he violated these "rules" in dealing with Examiner Chen during the several days of intense exchanges over the phone and via email (or in written communications then or thereafter). None of these were intentional. Indeed, the undersigned would welcome a telephone discussion with Examiner Chen if she has the time and inclination, in which she could point out more specifically what personal exchanges, or what written communication, she found unacceptable, so he can correct his manner (that was obviously perceived differently by her than he intended). The undersigned conveys his personal apologies to Ms. Chen for any tone, statements or written expressions that were offensive to her.

IV. Conclusion

In conclusion, it is respectfully requested that the above amendments, remarks and requests be considered and entered. Applicant respectfully submits that their amendments and remarks have overcome all the pending grounds for rejection and that all the present claims are in condition for allowance. It would further be proper to rejoin claims 54-72 at this time. Applicants respectfully request early notice of such favorable actions.

Examiner Chen is respectfully requested to contact the undersigned at (202) 496-7845 with any questions or comments if this will assist in understanding this amendment and response.

In the unlikely event that the Patent and Trademark Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due to **Deposit Account 50-0911**.. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: 11 July 2006

Shmuel Livnat
Registration No. 33,949

Direct Line: (202) 496-7845

MCKENNA LONG & ALDRIDGE LLP
1900 K Street, N.W.
Washington, DC 20006
Telephone: (202-496-7500
Telefax: (202) 496 7756
Attorneys for Applicant